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A

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6) Documents cited

Nature 1982, 299, 178-180

8) Field of search

C3H

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London SE1 6BU

## (54) Genetic engineering

(57) It has been a problem to find an alternative, less time-consuming, and more reliable source of factor IX, a polypeptide which is essential to the human blood-clotting process and necessary for the treatment of patients with Christmas disease. In order to aid in the solution of the problem, there is provided recombinant DNA containing a DNA sequence occurring in the human factor IX genome, and includes recombinant DNA comprising substantially the whole sequence of human factor IX genome, which is

inserted in a cloning vehicle and transformed into a host, such as *Escherichia coli*. Other fragments of the sequence have also been used and the invention includes DNA molecules comprising part or all of human factor IX DNA. There is also described cDNA derived from human factor IX RNA. Uses include the provision of an intermediate product in the genetic engineering of a factor IX polypeptide precursor and the manufacture of the factor IX polypeptide, and in making products for use in diagnosing the presence of normal or abnormal factor IX in patients with Christmas disease.

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1st amino acid  
sequence :

70 75  
Glu-Cys-Trp-Cys-Gln-Ala

mRNA :

5' GA<sup>A</sup><sub>G</sub> UG<sup>U</sup><sub>C</sub> UGG UG<sup>U</sup><sub>C</sub> CA<sup>A</sup><sub>G</sub> GCN 3'

Deoxyoligonucleotides  
synthesized :

3' CT<sup>T</sup><sub>C</sub> AC<sup>A</sup><sub>G</sub> ACC AC<sup>A</sup><sub>G</sub> GTT CG (oligo N2A)

3' CT<sup>T</sup><sub>C</sub> AC<sup>A</sup><sub>G</sub> ACC AC<sup>A</sup><sub>G</sub> GTC CG (oligo N2B)

2nd amino acid  
sequence :

348 352  
His-Met-Phe-Cys-Ala

mRNA :

5' CA<sup>U</sup><sub>C</sub> AUG UU<sup>U</sup><sub>C</sub> UG<sup>U</sup><sub>C</sub> GCN 3'

Deoxyoligonucleotides  
synthesized :

GT<sup>A</sup><sub>G</sub> TAC AA<sup>A</sup><sub>G</sub> AC<sup>A</sup><sub>G</sub> CG (oligo N1)

*Fig. 1*

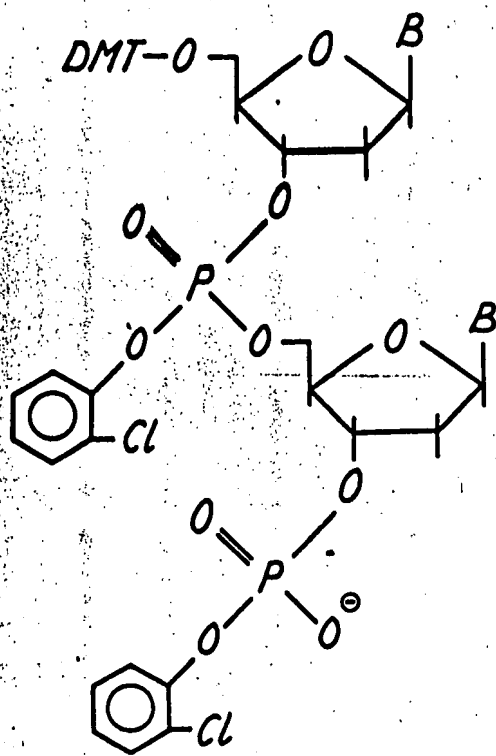


Fig. 2

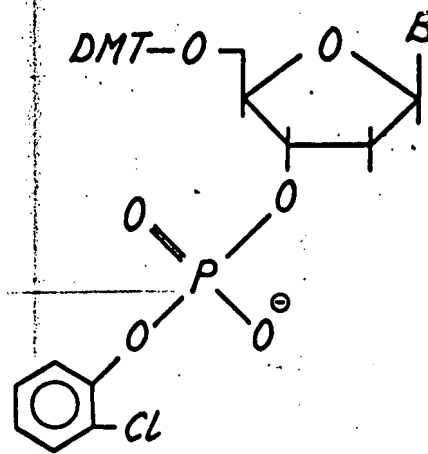


Fig. 3

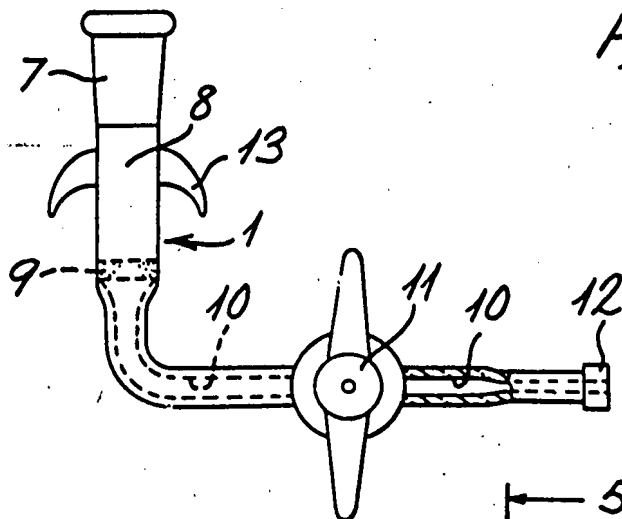
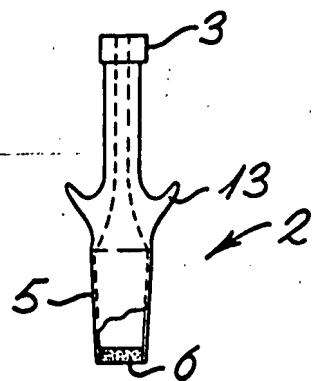


Fig. 4

5' TGAATCCAATCCATGTTTAAATGGCGGCATGTGCAAGGATGACATTAATTCCTAT  
10 20 30 40 50

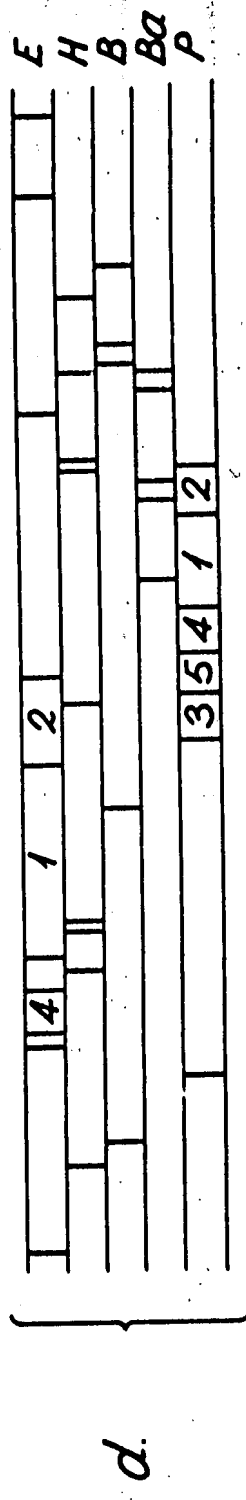
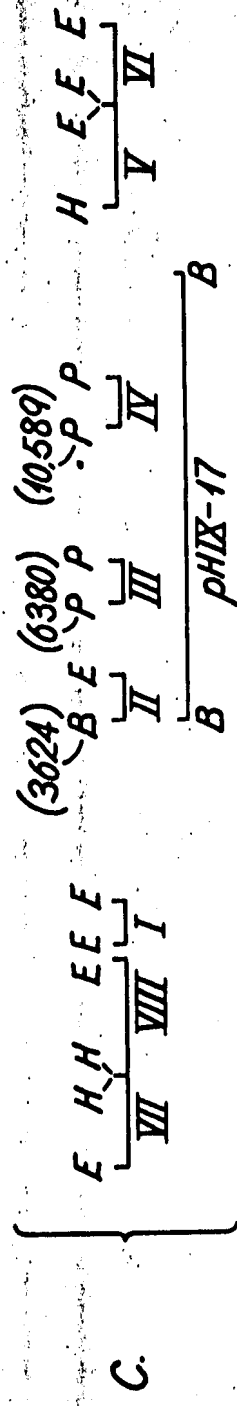
70 E C W C Q A G F E G T N C E L D A T C S I K  
80  
90  
GAATGTTGGTGTCAAGCTGGATTTGAAGGAACGAACTGTGAATTAGATGCAACATGCAGCATTA  
60 70 80 90 100 110 120

100 N G C K Q F C K R D T D N K V V C  
130 140 150 160 170

110 S C T D G Y R L A E D Q K S C E P A V P F P  
120  
130  
TCCTGTACTGACGGATACCGACTTGCAGAAGACCAAAAGTCCTGCGAACCAGCAGTGCCATTTC  
180 190 200 210 220 230 240

140 C G R V S V S H V R P R F H G L C S C \* E  
150  
CTGTGGACGAGTCTCTGTCTCACATGTGAGGCCCGCTTTCACGGTCTGTGTTTCGTGCTGAGAA 3'  
250 260 270 280 290 300

Fig. 5



4 2 3 4 5 6 7 8 9 10

Fig. 6

**FIG. 7a**

AGSCAAAGACACATAGTGCACCTATGASCCCAAGGCAATTCAAGGATACACCCATAGGAGGCTGGTTGACATCCACCAGAGCTAATCACCACCACATGCTGGAAAAAGACACAGGTGAAGC  
1090 1100 1110 1120 1130 1140 1150 1160 1170 1180 1190 1200

TGAGAAGAATGAAGTGGTGCATAGGAGGTATCTAATACAGTCACCTCATTTTCAAACTTTCCATGTTATGATTGCACAGACCACCTGAGGATTTCTATTGAAAGTTTTTACTGTGTGTCAAAC  
1210 1220 1230 1240 1250 1260 1270 1280 1290 1300 1310 1320

ACGTACACAAGGGGAAGGTGCTCTTACATTTGTTATGTTCTGCTGCTCTAGAAACAGAAA TAGGCTCAAGGCAGAGCCTGTTTTCTTAATTCAGCAGGTCTAACTAACCAAGTCTCT  
1330 1340 1350 1360 1370 1380 1390 1400 1410 1420 1430 1440

GAAACATGCTACTTCCTGTTATTTGGTATTGTCATAGGAGAAACAAAGGAAAGCACAGTAATTAGAAAATACAAAACAAGATGGCAGGAAATAGCCAAAAATATCAGGAACACAAATTTT  
1450 1460 1470 1480 1490 1500 1510 1520 1530 1540 1550 1560

GTGAATTGGGATTAAACTAATCTATTATATGACAACTTTTCAGCTTGGAGTTAAAAATTTAATTTGTATCTGTTAACGAAAGTGATACCTAAAAATAAAATTTACACCTGGGAGGCCAAAAAT  
1570 1580 1590 1600 1610 1620 1630 1640 1650 1660 1670 1680

GAGGGATGTGAAAGAACATATCAGGTAAAACTAACAAAAGAACTAGCAAGCAATCTTAATATCAGACAAAATAGATTCAAGAGGAAAAATCATTTTCAAAAAGACAAAGAGATTTTTTTT  
1690 1700 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800

TATTAATAAGGGGAATTGCATAGGAGAGTAAAGAAATGTGGCCACTGGAAATCTTAGCACTAATGACATATTGGTCTTTTGGTCTTCAGTTACCTTACAGGACCCTATTTTCAATTTCTCTT  
1810 1820 1830 1840 1850 1860 1870 1880 1890 1900 1910 1920

ATGTTTGATATGTAAACCCTCAGCCAGCTTCAAGTTGCTTTTGGCCCTAATGGACTTCCTAGCACTATAATTTCTTTTTTTTAAATGTTTTTATTTTAGGTTTAGGGGTACATGTGAA  
1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030 2040

GTTTGTACATAGATACATGTGTCTACAGGGGTTTGTTGTACATATTATACATGACGCAGATATTTCAGCTCAGTACCAAAATAGTGATCTTTTCTGCTCCCTCCTCATCCCCACCT  
2050 2060 2070 2080 2090 2100 2110 2120 2130 2140 2150 2160

[illegible]

**FIG. 7c**



AATTTATATTCATAAATTGCGAGAAAGGCAAAATTTCTTTAAATACAAAAGTGATCACCATAAAGGAAAAGATTGATAAACTGGACTATATTTAAACTAAGGACTCCTGTTTCAGCAAAAG  
3370 3380 3390 3400 3410 3420 3430 3440 3450 3460 3470 3480 3490  
ACACTACTTCGACTGAAAGACAAAGTCACAGAGTGAGACAAAGATATCTGCAATACAGATACCTAATAACTGAACCCCATACAGTGATGGGGAATTTAAGTTTCGTACAATCATTTTAGA  
3490 3500 3510 3520 3530 3540 3550 3560 3570 3580 3590 3600  
AAATTCCTTGGCAGTAAATCTACTAGATCTGAAACATGTGATCCAGTAATTACACTCATATAATTAT AAGCLGTAAAAAGGCATGTTTATGTCCACCAAAAGATATATACAAGAATGTTTCATTA  
3610 3620 3630 3640 3650 3660 3670 3680 3690 3700 3710 3720  
CACTATTATACATAAAGGCCAATAAATCTGAAACAAACCAAAATATCCATTAAACAGTAGAATGAA TAAATAAAAAGCTGTAATAGTAATAACAGTGGAACTACTACACAGCAATGTAAATGAACCT  
3730 3740 3750 3760 3770 3780 3790 3800 3810 3820 3830 3840  
ACTGCTGTACAAACAACTGGTTTAATCTCACAGACAAAATGTTAAATGAAGACACAGACGAGTACATATTGCGAACTTCTGTTTATAATTCAGAACTGGCAAGAACTSTTTTACTGT  
3850 3860 3870 3880 3890 3900 3910 3920 3930 3940 3950 3960  
GTTAAGTCCAGTAAATGGTAACCTATAAAGGAAAAGGATGGAATGATTGGAGGGGGCATCTTCTGGGGTATTGATAATGTGCTATGTATTGGTCAGTTTAGTTGTTTAAACAGGC  
3970 3980 3990 4000 4010 4020 4030 4040 4050 4060 4070 4080  
TCATTTTACTTTSTGAACAACTTACCTAAATTTGTTGTTATATGTTATACATTAAATAATAGGGTTTTTAAACCTGTAGTTTCATAATTTTAGTGAAAGTAGAATATCCAAA  
4090 4100 4110 4120 4130 4140 4150 4160 4170 4180 4190 4200  
CATTTAGTTTTAAACCAATCAATATAGTGCTACCATCATTTTTTATGSCATTATTGASAAAGTTTATTTTACCTTTCTTTCCACTCTTATTTCAAGGCTCCAAAATTTCTCTCCCCAACGTA  
4210 4220 4230 4240 4250 4260 4270 4280 4290 4300 4310 4320  
TATTGGGGCAACATGAATGCCCCCAATGTATATTGACCCCATACATGATGAGTCAGTAGTTCCATGTACTTTTTAGAAATGCCATGTTAAATGATGCTGTTACTGTCTATTTTGGCTTCTTTTA  
4330 4340 4350 4360 4370 4380 4390 4400 4410 4420 4430 4440  
ID V T C H I A N S R C E Q F C K N S A D N K V V C S C T E G Y R L A E N Q K S C  
GATGTAACATGTAACATTAAAGATGCGAGCAGTTTTTGTAAATAATAGTGCCTGATACAAAGGTGTTTGGCTCTGACTGAGGGATATCGACTTGCAGAAAACCAGAAAGTCTGT  
4450 4460 4470 4480 4490 4500 4510 4520 4530 4540 4550 4560

FIG. 7d

GAACCAAGCAGTCATATCTGAATAAGATTTTTTAAGAAATCTGTATCTGAACCTTCAGCA TTTTAACAACCTTACATAATTTTAATTCCTACTTGAATCTGCTTCCTTTTGAAATCA  
4570 4580 4590 4600 4610 4620 4630 4640 4650 4660 4670 4680

TAGAAAATATCAGTAGCTTGAATTAGACCAATTAATTTTCTAGATTGCATCATATTTTAAATAAAL ATGTAATCATCTACAACCTGAATTCCTTCTGAGTCCAATTTGTCCAATTTT  
4690 4700 4710 4720 4730 4740 4750 4760 4770 4780 4790 4800

TTTCTCTAACATTTATATCACAAAGCAATTAATTTGTGTGATTTCTGCATATGTATTTTCTAATTCATCAAGTCAAAATCAATGTAGTAATACTATATCATAAAAATATACACAAATAATTGA  
4810 4820 4830 4840 4850 4860 4870 4880 4890 4900 4910 4920

GTGATAGGCTTCTAGTATAAGGACGGTAAGTTTGAAGCATGATCTCTATCTGGCTGGCTAGTTTACTCTGAGAAAGTTATTTTTTATTTGTTGGTCTTAAAGCTGAGTTTACACACTTGGT  
4930 4940 4950 4960 4970 4980 4990 5000 5010 5020 5030 5040

GTCAGAAATGATTCGGGCAATGAACCTGTTTTATGTTCTGCTAGGCTGATCAGCACAACTATATGGCTGTGAACAAACAAATGTTTCCAGTCATACCAACCATGCCACCATTTTAACAGC  
5050 5060 5070 5080 5090 5100 5110 5120 5130 5140 5150 5160

TGATTAGTGTATTCAGAACATCTCCACTCCATGTTCTGATGGCTGTTATCTAAAGATGAAAGCAGTAGACACTTTTATTTTTTGA AAAATTTAGGCTCTGCAGGGTCAATTTATATTGAT  
5170 5180 5190 5200 5210 5220 5230 5240 5250 5260 5270 5280

AAATGAGGGCTTTTTTGAAGCAAACTAGATATAATTTCTTTTGTCTTAAAGCTGATATCTTATTAAATTTGGTACATTAAATTTGTGCACCATTTCTCTGTAACTGTTTCAGTACCTG  
5290 5300 5310 5320 5330 5340 5350 5360 5370 5380 5390 5400

TCTCAGCACTATACCAGGCAGAAAGAAATTAAGAAAGAACCAAGTCCGAGATCAGCTTGGTCAGGGAGACCCCTAATCTCGGCACTAGAGGAATTAAGACACACACAGAAATATA  
5410 5420 5430 5440 5450 5460 5470 5480 5490 5500 5510 5520

GATATGAAGTGGGAATCAGGGGCTCTCACAGCCTTCAGAGCTGAGAGCCCCGAAACAGAGATTTACCCACATATTTATTGACAGCAAGCCAGTCATAAGATTTACTGAAAGTATTCTCTTA  
5530 5540 5550 5560 5570 5580 5590 5600 5610 5620 5630 5640

TGGGAAATAAAGGATGATCTGGCTGTTATCTGTCAGCAGGAACATGTCCTTAAGGCACAAATCATTATGCAATTTGCTGTGGTTTAAAGAACACCTTTTAAGCAGTTTTCGCCCTTGGT  
5650 5660 5670 5680 5690 5700 5710 5720 5730 5740 5750 5760

FIG. 7e

4GCAGCAGAGTCCCATTTACCAAAATTGGAAAGT-AAAATTACAAAGCATCAATCATCAGACTTCCATTTCAGGGGATGGCAATTGGGAGTAAAGACTTTTTTAGTAAAGAAACTAAACACAAA  
4785 4790 4795 4800 4805 4810 4815 4820 4825 4830 4835

GTCATTAGACTCTATAAAGTCTTACCAJATTTGJYTCGGAAACCCATTCTATTCTCCTATTTCCGTAAAGATGATGAATTCGGAGCCAAAATGTYCTTTTTCATGGAAGGATTTGAAAACTGTCCBT  
6350 6356 6970 5830 6290 5900 6910 5920 6930 6940 6950

6970 6980 6990 7000 7010 7020 7030 7040 7050 7060 7070 7090

GAAATAACSCAATCAACCCTTTAGCTTGAGACTCTATTTCACCTGATTAGATTTTTTAAATAC TGATGGCC GCTTCTCAGAAGTGAC AAGGATGGGCCCTCAATCTCAATTTTTTGTAAAT

	V	P	F	P	C	G	R	V	S	V	S	Q	T	S	K	L	T	R	A	E
ACATGTTCCATTTGCCAATGASABATATCAGGTTACTAATTTTTCTCTATTTTTCTAGTGCCATTTCCATGTGGAGAGATTTCTGTTTCACAAACTTCTAAGCTCACCCGTGCTGAGGC	7090	7100	7110	7120	7130	7140	7150	7160	7170	7180	7190	7200								

V E P D V D V V N S T E A E T I L D N I T Q S T Q S F N D F T R V V G G E D A K  
 .TGT.TTTTCCCTGATGTGGACTATGTAATCTACTGAAGCTGAACCATTTTGGATAACATCAC TCAAGCACCCCAATCATTTAATGACTTCAC TCGGGTGTGTGGAGAGATGCCAA  
 7210 7220 7230 7240 7250 7260 7270 7280 7290 7300 7310 7320

P	G	C	P	M	Q
ACCAGGTC	AA	TT	CC	TT	GG
7220	7220	7220	7220	7220	7220
TTTAT	ACT	GTG	TC	AA	ACT
7330	7330	7330	7330	7330	7330
GATG	CTG	CTG	CTG	CTG	CTG
7360	7360	7360	7360	7360	7360
GGAG	CTC	AGCT	GG	AG	CT
7370	7370	7370	7370	7370	7370
GCAG	AC	AG	AC	AC	AG
7380	7380	7380	7380	7380	7380
AGCC	AG	CC	AG	CC	AG
7400	7400	7400	7400	7400	7400
GGAG	ACT	GAG	CT	GAG	CT
7410	7410	7410	7410	7410	7410
CTAT	TTT	ACT	AG	AC	AG
7420	7420	7420	7420	7420	7420
CTAT	TTT	ACT	AG	AC	AG
7430	7430	7430	7430	7430	7430
ACCT	ATT	GGG	GA	CT	ATT
7440	7440	7440	7440	7440	7440
TTGG	GA	CT	ATT	GG	GA
7450	7450	7450	7450	7450	7450

TGTGAGAGTGATTTAGGCACGTTTCAGCCACTAACCAATGTGAGAAGGCCCTCCAGAGATGAGCAGTGGTGAAGAGAGGCGCTCAAACCAGCTACCATACAGGTC	7450	7460	7470	7480	7490	7500	7510	7520	7530	7540	7550
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Sequence	7570	7600	7630	7660	7670
TAA GGA A A C A G C A T A G C A G G A T T C C A G A C A G S C A --- G S T C A A C A A C A T G A A G S T C T G S A A G A A A G G T C G C A G G T A C T C A G G T T C A G G G C A C T A C T T C A G C T T C A G C C C T T C A G C A A A A C T	7570	7580	7590	7600	7610
	7620	7630	7640	7650	7660
	7670				

GGTGAGGTTGGAAAGTCTTTAGGCTAAGAAAAATTCGATTATTTAAAGCGGCTAAAGAAAGGACCTCAAGGAGGAAGGATTAAGGCAAGAACTAGGTT-CAGGAACAGGGCATGAGAT  
7690 7700 7710 7720 7730 7740 7750 7760 7770 7780 7790 7800

ASAGTC	TTGAT	CTAC	CACTA	TAGT	TCTC	GT	-----	GGACT	CAAC	GGAG	ATTAC
7810	7320	7830	7840	7350	7860	7370	-----	7900	7910	7920	

TAACCGA-4TTTGA-AAC-CCTGG-CAACACG-CGAACCCACCTCTAATTAAAAAATACA AAATTAGGTAGGTGATGACTCCACCTGCTCCAGGCTATTCAGGAGGCTGAG

29

TGGGAGAAATCACTGAGCCTGSAAGTCGAGGCTGCAGTGAATTGTGATCACACCACCTGCACCTTCAGCCTGACTGACAGAGTAAGACCCCTATCTCAAAAAACGAAAAAGAAAAACACTG  
 8050 8060 8070 8080 8090 8100 8110 8120 8130 8140 8150 8160

SCCAAGGAAATGAACCTGTACAGAGCCCGGGTTCAAAAACACCAAAATATGCACCTTGACCTAGTCCTTCCCGGGTCTCTGCAGACATTTCTCCAAGCGTAGTCTGCAAAACAACCT  
 8170 8180 8190 8200 8210 8220 8230 8240 8250 8260 8270 8280

ACATATGTAGAAATTACCTATGCACATTTTTCATTTAACAAACCAG-GCTACATTTGTAGCAAAAATCTGGGTTGTAACCTTAGCCTACAGCTGAAGCCTAAGAGATTCCGTCTGTGAGAAGA  
 8290 8300 8310 8320 8330 8340 8350 8360 8370 8380 8390 8400

AATAACCCACCTCTTTGGCCCCCTCCCGAGGAGGAGCCAGGATGTCCTTATATAAAGTTGTCTGT-CAATAGGTAACCACTAGCCACATATG--TTTAAATTTTAAATTAACATACA  
 8410 8420 8430 8440 8450 8460 8470 8480 8490 8500 8510 8520

ATTAGAGAAATTAAATTCATTC-TCAATTGACCTGCCCAAATTTAAGCACATTAACAACACACATGTGG-TAGTAACACTACTGTATTGGAGAGTGCAGCGGAGATAGAACACTCTAT  
 8530 8540 8550 8560 8570 8580 8590 8600 8610 8620 8630 8640

TACTGCAGAAATTCCTATTGG-TAGCAGTTATATAGTTAGTGTAACTTAAACT-CCTAGTTGCCACAAGTCATGATTAGTAGTAATTTTCATGGA-----  
 8650 8660 8670 8680 8690 8700 8710 8720 8730 8740 8750 8760

-----  
 8770 8780 8790 8800 8810 8820 8830 8840 8850 8860 8870 8880

-----  
 8890 8900 8910 8920 8930 8940 8950 8960 8970 8980 8990 9000

-----  
 9010 9020 9030 9040 9050 9060 9070 9080 9090 9100 9110 9120

-----  
 9130 9140 9150 9160 9170 9180 9190 9200 9210 9220 9230 9240

FIG. 7h

-----CCC TATTCAAC CACATGAACAGATTAC TGATGTGACAGATTCAAGCCTTTTATCTTTCCAAAGGCAAGAGCTGAGCTACTTTCCAGATAGTTGTGAAAGACCCCTGTCTCA  
10210 10220 10230 10240 10250 10260 10270 10280 10290 10300 10310 10320

FIG. 7i

10330 10340 10350 10360 10370 10380 10390 10400 10410 10420 10430 10440  
AATGAAAGAACAGAAATCTCTCCTCATTTGTGGA TGGCCAGCTCCACCA TGTATGTTAA TCTGCAGGAGGAAATACTAGATTGATTCAGATCAGACTGCAGCAAACTGCTGT  
10450 10460 10470 10480 10490 10500 10510 10520 10530 10540 10550 10560  
GACTAAGGCATCAGAGAAAGCAAGCAACAGCTGGGGCTTCAGTGGTGAAACATTATATATCTAGCTTTG ATATGAAATACTGTTTAGCAGTGTCCACCTAGAAAAGAGTGTTCAAAA  
10570 10580 10590 10600 10610 10620 10630 10640 10650 10660 10670 10680  
TCTGATGCAACCTTTCTCTTCAGAGTTGTTTCTTTTATCTTTCAAAATTTAGCCAGGGTGGGAAATAAAGTGATCCTTGCTGGAAGAAATCTCACAAAGAAAGACATAGAGAGTTCACCTT  
10690 10700 10710 10720 10730 10740 10750 10760 10770 10780 10790 10800  
TCACTCGGAGTATGAAACAACTAGAAATGTTAGTCTGTTAAGAAAGGTGTAGGTGAGCTGTTTGCAGAGCCACAGGAAAGGGGAAAGACAACTTCTTTGTGGGACT  
10810 10820 10830 10840 10850 10860 10870 10880 10890 10900 10910 10920  
TAAGGCTGAAAGTTGCAAGCAGGCAAGACGATTCTGACCTCCATTAAAGAAA JCCCTTTCCAAACCAACCACTGGGTTGTTACACAGGTTGGGCAGCATTGGGAGCAAAATGTTGATTG  
10930 10940 10950 10960 10970 10980 10990 11000 11010 11020 11030 11040  
AACAAATGTTGTGGGAATGTTGACTTAAAGAGC GTTCTGTCTCACTGGGACAGCGGCTAGATAGCCCCCATTCAGGGAG-GGGCAATTTGTTTCACCTGGCCAGAGATCAGAGCAGGCTAA  
11050 11060 11070 11080 11090 11100 11110 11120 11130 11140 11150 11160  
GG-ACT-CTGGATCTGTCCAGCTTTGAGACCCCTACAGAGCCCATGTTCTCC TAGCACGTATCCCGTCTGCGGTACCGGTCAATTTCTTACCTTATTCAGGGCTTTTCACCTCAGCTTGCCA  
11170 11180 11190 11200 11210 11220 11230 11240 11250 11260 11270 11280  
GGCTGGAGCCAAAGGCAACGACGCGC-CTTGTTCGGATGGTAGCTTCCAGGAGCCCCCTATGTTTCCGGAACGGCGTG--CCCATCTCTGTTTGGCTACCTCCTAAAGCCAAAGG--C  
11290 11300 11310 11320 11330 11340 11350 11360 11370 11380 11390 11400  
TGGCGGG-C-GG-C---CTTCTAAAGTCGCGCAAGGTTAGAAAGGTTCCGGACAGGAACGGCGGTGAGGGCCAAATGGAAGGAGGTACTTCAGTTTCCCTCCAGGGCCCGCGGATGGGCTCAGA  
11410 11420 11430 11440 11450 11460 11470 11480 11490 11500 11510 11520

FIG. 7j

GCTCCTTSAGAACTCGGGAAGGAAAGCAGGGTCTCTGAAGAAAATACTTCAGSAGTAGAAGAGGAAGCTAGAGGGTTAAATGCCACTACACAGGAACAGAAATGAGTTTTTCTTAGAGTTA  
11530 11540 11550 11560 11570 11580 11590 11600 11610 11620 11630 11640

GTATATGTCTASAGGTGTAGTAAACTAAACCAAGTCTTTGAATTTGCATACCGCCACGTCAGGGAAAGAAATGAAAACCTTTTGAATATTAGTGAAAAAGGGAAACTSCAACGCCCTGTATTACT  
11650 11660 11670 11680 11690 11700 11710 11720 11730 11740 11750 11760

AGATAGCTTTTCATCAACGGCTCAAAACCCGACAGATTTAAAGAAACCAACCCGCTTTTGGCTTCTAAAGCTTTAAATTTGGTTTGGATCCCATGCCCATGACCCTGCCAGCTG

11770 11780 11790 11800 11810 11820 11830 11840 11850 11860 11870

FIG. 7k



FIG. 8(a)

→ 1 0.000  
 30 0.002  
 33 0.003  
 46 0.004  
 48 0.004  
 50 0.004  
 89 0.007  
 94 0.008  
 95 0.008  
 112 0.009  
 120 0.010  
 120 0.010  
 123 0.010  
 123 0.010  
 134 0.011  
 148 0.012  
 173 0.014  
 181 0.016  
 204 0.017  
 247 0.021  
 265 0.022  
 266 0.022  
 266 0.022  
 305 0.026  
 376 0.032  
 417 0.035  
 425 0.036  
 426 0.036  
 465 0.039  
 488 0.041  
 517 0.043  
 523 0.044  
  
 559 0.047  
 578 0.049  
 590 0.050  
 621 0.052  
 652 0.055  
 → 732 0.062  
 733 0.062  
 781 0.066  
 788 0.066  
 816 0.069

ECOR1  
 HINF1  
 MB011  
 ALU1  
 DDE1  
 MNL1  
 MNL1  
 MST1  
 MHA1  
 MB01  
 98V1  
 FNU4H1  
 BBV1  
 FNU4H1  
 DDE1  
 HPH1  
 MNL1  
 DDE1  
 HINF1  
 SPH1  
 ALU1  
 BBV1  
 FNU4H1  
 XMN1  
 ALU1  
 MNL1  
 STU1  
 HAE111  
 RSA1  
 DDE1  
 ALU1  
 ALU1  
  
 MNL1  
 RSA1  
 DDE1  
 ALU1  
 HINF1  
 HIND111  
 ALU1  
 MB011  
 MNL1  
 MNL1

GAATTC  
 GAATC  
 TCTTC  
 AGCT  
 CTGAG  
 GAGG  
 CCTC  
 TCGCA  
 GCGC  
 GATC  
 GCAGC  
 GCAGC  
 GCAGC  
 GCAGC  
 CTGAG  
 GGTGA  
 GAGG  
 CTTAG  
 GAATC  
 GCATGC  
 AGCT  
 GCTGC  
 GCTGC  
 GAACACTTTC  
 AGCT  
 GAGG  
 AGGCCT  
 GGCC  
 GTAC  
 CTTAG  
 AGCT  
 AGCT  
  
 CCTC  
 GTAC  
 CTAAG  
 AGCT  
 GATTC  
 AAGCTT  
 AGCT  
 GAAGA  
 GAGG  
 GAGG

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FIG. 8(b)

818 0.069  
 898 0.076  
 898 0.076  
 899 0.076  
 913 0.077  
 929 0.078  
 976 0.082  
 1027 0.086  
 1032 0.087  
 1054 0.089  
 → 1072 0.090  
 1073 0.090  
 1099 0.092  
 1099 0.092  
 1101 0.093  
 1138 0.096  
 1145 0.096  
 1150 0.097  
 1161 0.098  
 1167 0.098  
 1193 0.100  
 1198 0.101  
 1200 0.101  
 1204 0.101  
 1226 0.103  
 1284 0.108  
 1286 0.108  
 1323 0.111  
 1365 0.115  
 1365 0.115  
 1370 0.115  
 1424 0.120  
 1427 0.120  
 1449 0.122  
 1603 0.135  
 1626 0.137  
 1663 0.137  
 1670 0.141  
 1672 0.141  
 1685 0.142  
 1759 0.148  
 1766 0.149  
 1841 0.155  
 1842 0.155

FOK1  
 MNL1  
 MST11  
 DDE1  
 DDE1  
 HPH1  
 TAQ1  
 RSA1  
 MNL1  
 MNL1  
 HIND111  
 ALU1  
 BBV1  
 FNU4H1  
 ALU1  
 MNL1  
 HINC11  
 FOK1  
 ALU1  
 HPH1  
 HPH1  
 ALU1  
 DDE1  
 MB011  
 MNL1  
 DDE1  
 MNL1  
 RSA1  
 BBV1  
 FNU4H1  
 XBA1  
 DDE1  
 ALU1  
 RSA1  
 ALU1  
 ACC1  
 HINC11  
 HPT111  
 MNL1  
 HAE111  
 FOK1  
 HINF1  
 MNL1  
 SAU961  
 HAE111

GGATG  
 CCTC  
 CCTCAGG  
 CTCAG  
 CTGAG  
 GGTGA  
 TCGA  
 GTAC  
 GAGG  
 CCTC  
 AAGCTT  
 AGCT  
 GCAGC  
 GCAGC  
 AGCT  
 GAGG  
 GTTGAC  
 CATCC  
 AGCT  
 TCACC  
 GGTGA  
 AGCT  
 CTGAG  
 GAAGA  
 GAGG  
 CTGAG  
 GAGG  
 GTAC  
 GCTGC  
 GCTGC  
 TCTAGA  
 CTAAG  
 AGCT  
 GTAC  
 AGCT  
 GTATAC  
 GGTAAAC  
 GTTAAAC  
 GAGG  
 GGCC  
 GGATG  
 GATTC  
 GAGG  
 GGGCC  
 GGCC

FIG. 8(c)

1855 0.156  
1884 0.159  
1901 0.160  
1901 0.160  
1939 0.163  
1940 0.163

DDE1  
MBO11  
AVA11  
SAU961  
MNL1  
DDE1

CTTAG  
TCTTC  
GGACC  
GGACC  
CCTC  
CTCAG

1947 0.164  
1965 0.165  
1965 0.165  
2030 0.171  
2081 0.175  
2097 0.177  
2110 0.178  
2112 0.178  
2116 0.178  
2128 0.179  
2141 0.180  
2147 0.181  
2150 0.181  
2158 0.182  
2161 0.182  
2165 0.182  
2171 0.183  
2174 0.183  
2222 0.187  
2225 0.187  
2248 0.189  
2282 0.192  
2283 0.192  
2287 0.193  
2296 0.193  
2301 0.194  
2349 0.198  
2349 0.198  
2422 0.204  
2468 0.208  
2483 0.209  
2503 0.211  
2524 0.212  
2534 0.213

ALU1  
HAE111  
SAU961  
RSA1  
RSA1  
HGA1  
ALU1  
DDE1  
RSA1  
MBO1  
MNL1  
MNL1  
FOK1  
MNL1  
MNL1  
MNL1  
MNL1  
ACC1  
HINF1  
DDE1  
ALU1  
PST1  
MST11  
DDE1  
FOK1  
MNL1  
ALU1  
BBV1  
FNU4H1  
HINF1  
HINF1  
BSTE11  
ALU1  
XBA1  
DDE1

AGCT  
GGCC  
GGCCC  
GTAC  
GTAC  
GACGC  
AGCT  
CTCAG  
GTAC  
GATC  
CCTC  
CCTC  
CATCC  
CCTC  
CCTC  
CCTC  
GTAGAC  
GACTC  
CTTAG  
AGCT  
CTGCAG  
CCTAAGG  
CTAAG  
GGATG  
CCTC  
AGCT  
GCTGC  
GCTGC  
GATTC  
GATTC  
GGTAACC  
AGCT  
TCTAGA  
CTAAG

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FIG. 8(d)

2658 0.224  
2678 0.225  
2726 0.230  
2728 0.230  
2770 0.233  
2807 0.236  
2811 0.237  
2965 0.250  
2984 0.251  
2984 0.251  
3012 0.254  
3024 0.255  
3032 0.255  
3048 0.257  
3090 0.260  
3093 0.260  
306 0.262  
3141 0.264  
3168 0.267  
3193 0.269  
3213 0.271  
3216 0.271  
3220 0.271  
3234 0.272  
3263 0.275  
3333 0.281  
3412 0.287

RSA1  
SFNA1  
HINF1  
HINC11  
HINF1  
HGA1  
DDE1  
HINF1  
AVA11  
SAU961  
MNL1  
HINF1  
ALU1  
NDE1  
MNL1  
MB011  
RSA1  
TAQ1  
RSA1  
MB01  
HGIA1  
DDE1  
MB011  
RSA1  
MNL1  
NDE1  
BCL1

GTAC  
GCATC  
GAGTC  
GTCAAC  
GATTC  
GACGC  
CTTAG  
GATTC  
GGTCC  
GGTCC  
GAGG  
GATTC  
AGCT  
CATATG  
GAGG  
GAAGA  
GTAC  
TCGA  
GTAC  
GATC  
GTGCTC  
CTCAG  
GAAGA  
GTAC  
GAGG  
CATATG  
TGATCA

3413 0.287  
3415 0.288  
3457 0.291  
3462 0.292  
3489 0.294  
3522 0.297  
3585 0.302  
→ 3624 0.305  
3625 0.305  
3638 0.306  
3689 0.311  
3792 0.319

MB01  
HPH1  
DDE1  
HINF1  
TAQ1  
ECOR5  
RSA1  
BGL11  
MB01  
MB01  
HPH1  
ALU1

GATC  
TCACC  
CTAAG  
GACTC  
TCGA  
GATATC  
GTAC  
AGATCT  
GATC  
GATC  
TCACC  
AGCT

FIG. 8(e)

3847	0.324	RSA1	GTAC
3905	0.329	RSA1	GTAC
3970	0.334	BSTN1	CCAGG
3970	0.334	SCRF1	CCAGG
3979	0.335	BSTE11	GGTAACC
4016	0.338	MNL1	GAGG
4022	0.339	SFNA1	GCATC
4025	0.339	M3011	TCTTC
4368	0.368	HINF1	GAGTC
4384	0.369	RSA1	GTAC
4410	0.371	SFNA1	GATGC
4469	0.376	SFNA1	GATGC
4520	0.381	RSA1	GTAC
4523	0.381	DDE1	CTGAG
4525	0.381	MNL1	GAGG
4529	0.381	ECORS	GATATC
4533	0.382	TAQ1	TCGA
4658	0.392	HINF1	GAATC
4695	0.395	ALU1	AGCT
4719	0.397	XBA1	TCTAGA
4727	0.398	SFNA1	GCATC
→ 4769	0.402	ECOR1	GAATTC
4769	0.402	XMN1	GAATTCCTTC
4778	0.402	DDE1	CTGAG
4780	0.403	HINF1	GAGTC
4848	0.408	NDE1	CATATG
4961	0.418	HINF1	GATTC
4988	0.420	DDE1	CTGAG
5020	0.423	ALU1	AGCT
5022	0.423	DDE1	CTGAG
5049	0.425	HINF1	GATTC
5053	0.426	HPA11	CCGG
5085	0.428	BCL1	TGATCA
5086	0.428	M201	GATC
→ 5157	0.434	PVU11	CAGCTG
5158	0.434	ALU1	AGCT
5225	0.440	ACC1	GATGAC
5258	0.443	PST1	CTGCAG
5285	0.445	MNL1	GAGG
5339	0.450	ECORS	GATATC
5355	0.451	RSA1	GTAC
5367	0.452	HGIA1	GTGCAC
5394	0.454	RSA1	GTAC
5402	0.455	DDE1	CTCAG
5414	0.456	BSTN1	CCAGG

FIG. 8(f)

5414 0.456  
5421 0.456  
5451 0.459  
5455 0.459

SCRF1  
MB011  
MB01  
ALU1

CCAGG  
GAAGA  
GATC  
AGCT

5481 0.462  
5490 0.462  
5560 0.468  
5562 0.468  
5627 0.474  
5653 0.476  
5657 0.476  
5672 0.478  
5674 0.478  
5674 0.478  
5754 0.485  
5754 0.485  
5761 0.485  
5762 0.485  
5764 0.485  
5764 0.485  
5779 0.487  
5813 0.490  
5821 0.490  
5844 0.492  
5844 0.492  
5845 0.492  
5863 0.494  
5864 0.494  
5875 0.495  
5876 0.495  
5886 0.496  
5887 0.496  
5898 0.497  
5899 0.497  
5900 0.497  
5922 0.499  
5952 0.501  
5955 0.501  
5961 0.502  
5971 0.503

FNU4H1  
MNL1  
ALU1  
DDE1  
XMN1  
FOK1  
HINF1  
PST1  
BBV1  
FNU4H1  
BSTN1  
SCRF1  
SAU961  
HAE111  
BSTN1  
SCRF1  
MNL1  
ECOR5  
HAE111  
BBV1  
FNU4H1  
PST1  
BAL1  
HAE111  
SAU961  
HAE111  
BAL1  
HAE111  
MNL1  
STU1  
HAE111  
ALU1  
MB011  
HINF1  
DDE1  
SAU961

GGGGC  
GAGC  
AGCT  
CTGAG  
GAAAGTATTC  
GGATG  
GAGTC  
CTGCAG  
GCAGC  
GCAGC  
CCTGG  
CCTGG  
GGGCC  
GGCC  
CCAGG  
CCAGG  
CCTC  
GATATC  
GGCC  
GCTGC  
GCTGC  
CTGCAG  
TGGCCA  
GGCC  
GGGCC  
GGCC  
TGGCCA  
GGCC  
GAGG  
AGGCCT  
GGCC  
AGCT  
GAAGA  
GAATC  
CTAAG  
GGGCC

FIG. 8(g)

5972	0.503	HAE111	GGCC
5987	0.504	MB011	TCTTC
5994	0.505	BSTN1	CCTGG
5994	0.505	SCRF1	CCTGG
6000	0.505	MB011	TCTTC
6021	0.507	ALU1	AGCT
6026	0.507	ACC1	GTCTAC
6037	0.508	MNL1	GAGG
6121	0.515	ALU1	AGCT
6139	0.517	MB011	TCTTC
6177	0.520	MNL1	CCTC
6211	0.523	DDE1	CTTAG
6214	0.523	ALU1	AGCT
6233	0.525	HAE111	GGCC
→ 6248	0.526	HIND111	AAGCTT
6249	0.526	ALU1	AGCT
6275	0.528	AVA11	GGTCC
6275	0.528	SAU961	GGTCC
6305	0.531	RSA1	GTAC
6361	0.536	MB011	TCTTC
6370	0.537	BBV1	GCAGC
6379	0.537	FNU4H1	GCAGC
→ 6380	0.537	PVU11	CAGCTG
6381	0.537	ALU1	AGCT
6558	0.552	AVA11	GGTCC
6558	0.552	SAU961	GGTCC
6561	0.553	BSTN1	CCTGG
6561	0.553	SCRF1	CCTGG
6564	0.553	HPH1	GGTGA
6629	0.558	HINF1	GAATC
6639	0.559	MB01	GATC
6674	0.562	HINF1	GAATC
6677	0.562	XBA1	TCTAGA
6683	0.563	STU1	AGGCCT
6684	0.563	HAE111	GGCC
6722	0.566	BBV1	GCAGC
6722	0.566	FNU4H1	GCAGC
6767	0.570	SFNA1	GCATC
6793	0.572	FOK1	GGATG
6848	0.577	HINF1	GACTC

FIG. 8(h)

6874 0.579  
6911 0.582  
6916 0.582  
6984 0.588  
6991 0.589  
7028 0.592  
7029 0.592  
7038 0.593  
7052 0.594  
7056 0.594  
7057 0.594  
7059 0.594  
7124 0.600  
7155 0.603  
7155 0.603  
7179 0.605  
7182 0.605  
7185 0.605  
7194 0.606  
7196 0.606  
7237 0.609  
7293 0.614  
7310 0.616  
7313 0.616  
7322 0.617  
7322 0.617  
7343 0.618  
7373 0.621  
7373 0.621  
7374 0.621  
7376 0.621  
→ 7378 0.621  
7379 0.621  
7394 0.623  
7396 0.623  
7396 0.623  
7408 0.624  
7410 0.624  
7438 0.626  
7485 0.630  
7486 0.630  
7488 0.631  
7507 0.632  
7516 0.633  
7529 0.634  
7547 0.636

HINF1  
ECOR1  
HPA11  
ALU1  
HINF1  
SAU961  
HAE111  
DDE1  
FOK1  
SAU961  
HAE111  
MNL1  
MB011  
MB011  
XMN1  
DDE1  
ALU1  
HPH1  
DDE1  
MNL1  
ALU1  
AVA1  
MB011  
SFNA1  
BSTN1  
SCRFF  
RSA1  
HGIA1  
SAC1  
ALU1  
DDE1  
PVU11  
ALU1  
HAE111  
BSTN1  
SCRFF  
DDE1  
MNL1  
FOK1  
STU1  
HAE111  
MNL1  
HPH1  
MNL1  
ALU1  
MRO11

GATTC  
GAATTC  
CCGG  
AGCT  
GACTC  
GGGCC  
GGCC  
CTCAG  
GGATG  
GGGCC  
GGCC  
CCTC  
TCTTC  
GAAGA  
GAAGAGTTTC  
CTAAG  
AGCT  
TCACC  
CTGAG  
GAGG  
AGCT  
CTCGGG  
GAAGA  
GATGC  
CCAGG  
CCAGG  
GTAC  
GAGCTC  
GAGCTC  
AGCT  
CTCAG  
CAGCTG  
AGCT  
GGCC  
CCAGG  
CCAGG  
CTGAG  
GAGG  
GGATG  
AGGCCT  
GGCC  
CCTC  
GGTGA  
GAGG  
AGCT  
GAAGA



FIG. 8(i)

7580	0.638	HINF1	GATTC
7599	0.640	HINC11	GTCAAC
7619	0.642	MB011	GAAGA
7634	0.643	RSA1	GTAC
7637	0.643	DDE1	CTCAG
7659	0.645	ALU1	AGCT
7681	0.647	HPH1	GGTGA
7705	0.649	DDE1	CTAAG
7745	0.652	HINF1	GACTC
7753	0.653	MNL1	GAGG
7802	0.657	HINF1	GAGTC
7809	0.658	MB01	GATC
7940	0.669	BSTN1	CCTGG
7940	0.669	SCR11	CCTGG
7963	0.671	MNL1	CCTC
7989	0.673	ALU1	AGCT
8002	0.674	HINF1	GACTC
8013	0.675	HGIA1	GTGCTC
8021	0.675	ALU1	AGCT
8031	0.676	MNL1	GAGG
8035	0.677	DDE1	CTGAG
8037	0.677	MNL1	GAGG
8046	0.678	HINF1	GAATC
8049	0.678	HPH1	TCACC
8053	0.678	DDE1	CTGAG
8058	0.679	BSTN1	CCTGG
8058	0.679	SCR11	CCTGG
8067	0.679	TAQ1	TCGA
8069	0.680	MNL1	GAGG
8072	0.680	BBV1	GCTGC
8072	0.680	FNU4H1	GCTGC
8073	0.680	PST1	CTGCAG
8086	0.681	BCL1	TGATCA
8087	0.681	MB01	GATC
8109	0.683	DDE1	CTGAG
8160	0.687	HAE111	GGCC
8160	0.687	SAU961	GGCCC
8190	0.690	HPA11	CCGG

FIG. 8(j)

8190 0.690  
8190 0.690  
8220 0.692  
8233 0.693  
8233 0.693  
8233 0.693  
8233 0.693  
8233 0.693  
8234 0.693  
8234 0.693  
8234 0.693  
8238 0.694  
8243 0.694  
8282 0.697  
8357 0.704  
8366 0.705  
8367 0.705  
8376 0.705  
8382 0.706  
8396 0.707  
8410 0.708  
8417 0.709  
8417 0.709  
8423 0.709

NCI1  
SCRF1  
RSA1  
AVA1  
NCI1  
SCRF1  
SMA1  
HPA11  
NCI1  
SCRF1  
HGIA1  
PST1  
NDE1  
DDE1  
PVU11  
ALU1  
DDE1  
HINF1  
MB011  
MNL1  
HAE111  
SAU961  
MNL1

CCGGG  
CCGGG  
GTAC  
CCCGGG  
CCCGG  
CCCGG  
CCCGGG  
CCGG  
CCGGG  
CCGGG  
GTGCTC  
CTGCAG  
CATATG  
CTTAG  
CAGCTG  
AGCT  
CTAAG  
GATTC  
GAAGA  
CCTC  
GGCC  
GGCCC  
CCTC

8428 0.710  
8428 0.710  
8440 0.711  
8440 0.711  
8443 0.711  
8447 0.711  
8447 0.711  
8477 0.714  
8492 0.715  
8643 0.728  
9221 0.777  
9263 0.780  
9266 0.780  
9294 0.783  
9335 0.786  
9350 0.787

BSTN1  
SCRF1  
BSTN1  
SCRF1  
FOK1  
AVA11  
SAU961  
BSTE11  
NDE1  
PST1  
MB01  
MNL1  
MNL1  
MNL1  
FOK1  
MB011

CCAGG  
CCAGG  
CCAGG  
CCAGG  
GGATG  
GGTCC  
GGTCC  
GGTAACC  
CATATG  
CTGCAG  
GATC  
CCTC  
CCTC  
GAGG  
CATCC  
TCTTC

FIG. 8(k)

9353	0.788	MB011	TCTTC
9394	0.791	BSTN1	CCTGG
9394	0.791	SCRF1	CCTGG
9406	0.792	MNL1	CCTC
9550	0.804	MB01	GATC
9571	0.806	MB011	TCTTC
9600	0.808	HGIA1	GTGCTC
9603	0.809	DDE1	CTCAG
→ 9614	0.810	SAMH1	GGATCC
9615	0.810	MB01	GATC
9626	0.811	BSTN1	CCAGG
9626	0.811	SCRF1	CCAGG
9641	0.812	ALU1	AGCT
9643	0.812	DDE1	CTAAG
9647	0.812	MB011	GAAGA
9676	0.815	HINF1	GATTC
968	0.816	MB01	GATC
9694	0.816	FOK1	CATCC
9697	0.817	BSTN1	CCTGG
9697	0.817	SCRF1	CCTGG
9723	0.819	MB011	TCTTC
9747	0.821	NCI1	CCCGG
9747	0.821	SCRF1	CCCGG
9748	0.821	HPA11	CCGG
9762	0.822	HAE11	GGCGCC
9762	0.822	NAR1	GGCGCC
9763	0.822	HHA1	GCGC
9777	0.823	ALU1	AGCT
9787	0.824	MNL1	GAGG
9791	0.825	DDE1	CTGAG
9793	0.825	MNL1	GAGG
9814	0.826	HPA11	CCGG
9814	0.826	NCI1	CCGGG
9814	0.826	SCRF1	CCGGG
9819	0.827	MNL1	GAGG
9826	0.828	ALU1	AGCT
9843	0.829	MB01	GATC
9864	0.831	BSTN1	CCTGG
9864	0.831	SCRF1	CCTGG
9881	0.832	HINF1	GACTC
10246	0.863	HINF1	GATTC
10279	0.866	ALU1	AGCT
10281	0.866	DDE1	CTGAG
10284	0.866	ALU1	AGCT
10310	0.868	TTM1111	GACCCGTGTC

FIG. 8(L)

10336 0.870  
10347 0.871  
10351 0.872  
10455 0.880  
10463 0.881  
10473 0.882  
10477 0.882  
10478 0.882  
10482 0.883  
10505 0.885  
10512 0.885  
10536 0.887  
10543 0.888  
10545 0.888  
10545 J.888  
10563 0.890  
10568 0.890  
10589 0.892  
10590 0.892  
10605 0.893  
10625 0.895  
10656 0.897  
10685 0.900  
10692 0.901  
10733 0.904  
10733 0.904  
10751 0.905  
10752 0.905  
10760 0.906  
10763 0.906  
10779 0.908  
10865 0.915  
10869 0.915  
10899 0.918  
10925 0.920  
10950 0.922  
10958 0.923  
11015 0.928

MNL1  
MNL1  
FOK1  
HINF1  
MNL1  
FOK1  
SAU961  
HAE111  
ALU1  
PST1  
MNL1  
M301  
PST1  
B3V1  
FNU4H1  
DDE1  
SFNA1  
PVU11  
ALU1  
HPH1  
ALU1  
HPH1  
SFNA1  
M3011  
BSTN1  
SCRF1  
ECL1  
ME01  
HPH1  
MB011  
MB011  
HPH1  
ALU1  
MB011  
HPH1  
HINF1  
MNL1  
B3V1

CCTC  
CCTC  
CATCC  
GAATC  
CCTC  
GGATG  
GGGCC  
GGCC  
AGCT  
CTGCAG  
GAGG  
GATC  
CTGCAG  
GCAGC  
GCAGC  
CTAAG  
GCATC  
CAGCTG  
AGCT  
GGTGA  
AGCT  
TCACC  
GATGC  
TCTTC  
CCAGG  
CCAGG  
TGATCA  
GATC  
GGTGA  
GAAGA  
GAAGA  
GGTGA  
AGCT  
GAAGA  
GGTGA  
GATTC  
CCTC  
GCAGC

FIG. 8(m)

11015	0.928	FNU4H1	GCAGC
11061	0.932	HINC11	GTTGAC
11073	0.933	ALU1	AGCT
11095	0.934	FNU4H1	GCGGC
11132	0.938	HPH1	TCACC
11135	0.938	BSTN1	CCTGG
11135	0.938	SCRF1	CCTGG
11137	0.938	BAL1	TGGCCA
11138	0.938	HAE111	GGCC
11145	0.939	MB01	GATC
11157	0.940	DDE1	CTAAG
11170	0.941	BAMH1	GGATCC
11171	0.941	MB01	GATC
11181	0.942	ALU1	AGCT
11256	0.948	BSTN1	CCAGG
11256	0.948	SCRF1	CCAGG
11265	0.949	HPH1	TCACC
11268	0.949	MNL1	CCTC
11268	0.949	DDE1	CTCAG
11272	0.949	ALU1	AGCT
11278	0.950	BSTN1	CCAGG
11278	0.950	SCRF1	CCAGG
11300	0.952	BBV1	GCAGC
11300	0.952	FNU4H1	GCAGC
11303	0.952	FNU4H1	GCCGC
11314	0.953	NRU1	TCGCGA
11315	0.953	FNUD11	CGCG
11324	0.954	ALU1	AGCT
11330	0.954	BSTN1	CCAGG
11330	0.954	SCRF1	CCAGG
11349	0.956	HPA11	CCGG
11356	0.956	HAE11	GGCGCT
11357	0.956	HHA1	GCGC
11367	0.957	FOK1	CATCC
11381	0.958	MNL1	CCTC
11428	0.962	FNUD11	CGCG
11429	0.963	HHA1	GCGC
11447	0.964	HPA11	CCGG
11464	0.965	MNL1	GAGG

FIG. 8(n)

11466	0.966	HAE111	GGCC
11478	0.967	MNL1	GAGG
11481	0.967	RSA1	GTAC
11494	0.968	MNL1	CCTC
11497	0.968	BSTN1	CCAGG
11497	0.968	SCRF1	CCAGG
11500	0.968	HAE111	GGCC
11500	0.968	SAU961	GGCCC
11504	0.969	FNUD11	CGCG
11505	0.969	HHA1	GCGC
11506	0.969	FNUD11	CGCG
11515	0.970	DDE1	CTCAG
11517	0.970	HGIA1	GAGCTC
11519	0.970	SAC1	GAGCTC
11520	0.970	ALU1	AGCT
11533	0.971	AVA1	CTCGGG
11557	0.973	MB011	GAAGA
11560	0.974	XMN1	GAAATACTTC
11581	0.975	MNL1	GAGG
11586	0.976	ALU1	AGCT
11591	0.976	MNL1	GAGG
11631	0.980	DDE1	CTTAG
11648	0.981	XBA1	TCTAGA
11652	0.981	MNL1	GAGG
11701	0.985	MB011	GAAGA
11765	0.991	ALU1	AGCT
11778	0.992	ALU1	AGCT
→ 11828	0.996	HIND111	AAGCTT
11829	0.996	ALU1	AGCT
11845	0.998	BAMH1	GGATCC
11846	0.998	MB01	GATC
→ 11868	0.999	PVU11	CAGCTG
11869	1.000	ALU1	AGCT

M I U A E S P G L I T I C L L G Y L L S A E C T V F L D M E N A M K  
 TTTTCTAGCAGATTG TGAACATGATCATGGCAGAA\* CACCAGGCCCTCATCACCATCTGCCTTTTAGGATATCTACTCAGTGCCTGAATGTACAGTTTTTCTTGATCATGAAAACGCCCAACA  
 10 20 30 40 50 60 70 80 90 100 110 120

I	L	N	K	F	K	F	Y	N	S	G	K	L	E	Z	F	V	J	G	N	L	E	R	E	C	M	E	E	K	C	S	F	E	E	A	R	E	V	F	E
AAATTCGATCGCCCAAAEAGGTATAATTTCAGGTAAATTTGGAGAGTTTTTCTCAAGGGAACCTTGAGAGAGCAATGTATGGAGAAGAAAGTGTAGTTTTYGAGGAAGCAGCAGAACGTTTTTG	138	140	142	144	146	148	150	152	154	156	158	160	162	164	166	170	172	174	176	178	180	182	190	200	210	220	230	240											

[illegible][illegible]

120										140									
G	A	C	T	G	A	C	T	G	A	C	T	G	A	C	T	G	A	C	T
AGGG	ATCG	AC	TTG	CAG	AA	AC	CA	AG	ATC	CTG	TA	CC	AG	CA	CTG	CG	AT	CC	AG
500	450	510	520	530	540	550	560	570	580	590	600								

160  
 L Y V W S T E A E T I L D A I T L S T Q S F N D F T R V V G G E D A K P G G F P  
 TGGACTTCTAAATTTCTACGTGAGCTGAACCATTTTGGATAACATCCTCATCAGCACCCCAATCATTTAATGACTTCACCTCGGTTGTGTGGAGAGATGCCAACCCAGGTCAATCC  
 610 620 630 640 650 660 670 680 690 700 710 720

	200	220
W Q V V L M C K V D A F C C G S I V K E K W I V T A A H C V E T G V K I T V V		
CTTGGCAGCTTTGATTGATGCA*TCCTGGAGGCTCTATCGTTAATGAAATGGATTGTAAC TCTGCCCACTGTGTGAAACTGGTGTAAATTTACAGTTGTCG	740	820
	750	830
	760	840
	770	
	780	
	790	
	800	
	810	
	820	
	830	
	840	

240  
 260  
 C E F M I E E T E H T E J K R N V I R I I P H H N Y N A A I N K Y N M D I A L L  
 CA C T G C A C A T A T T G A G G A C A G A C A T A C A F A C C A A A G C G A A T G T G A T T C G A A T T A T T C T C A C C A C A C T A C A A T G C A G C T A T T A A T A G T A C A A C C A T G A C A T T G C C C T T C  
 F50 86C 870 880 890 900 910 92J 930 940 950 960

→ 280  
L C E F L V L N S Y V T F I C I A D K E Y T N I F L K F G S G Y V S G W G R V

300

FIG. 9(b)

340  
F M K S A S L V L S Y L R V P L V D R A C L R S T K F T I Y N M F C A G F  
1050 1100 1110 1120 1130 1140 1150 1160 1170 1180 1190 1200  
1210 1220 1230 1240 1250 1260 1270 1280 1290 1300 1310 1320  
380  
M E S G H D S L S G D S G G P H V T E V E G T S F L T G I I S W G E E C A P K  
1210 1220 1230 1240 1250 1260 1270 1280 1290 1300 1310 1320  
415  
A Y G I V T V S S Y V N W I K E K T K L T \*  
1230 1240 1250 1260 1270 1280 1290 1300 1310 1320 1330 1340  
440  
G C A A T A T G G A A T T T A C C A A G G A T C C G G Y A T C I C A A C T G G A T T A A G G A A A A C A A A G C T C A C T T A A T G A A G A T G G A T T C C A A G G T T A A T T C A T T G G A A T T G A A A A T T A A C A G G  
1230 1240 1250 1260 1270 1280 1290 1300 1310 1320 1330 1340  
470  
G C C I C A C T A A C T A A T C A C T T T C C C A T C T T T T G T T A G A T T T G A A T A T A C A T T C T A T G A T C A T T G C T T T T C T T T T A C A G G G A G A A T T C A T A T T T T A C C T G A G C A A T T G A T T A G  
1450 1460 1470 1480 1490 1500 1510 1520 1530 1540 1550 1560  
500  
A A A T G G A A C C A C T A G A G G A T A A T S T G T T A G G A A T T A C A G T C A T T T C T A A G G G C C C A G C C T T G A C A A A T T G T G A A T T A A T T C C C A C T C T G T C C A T C A G A T A C T A T G G T T C T  
1570 1580 1590 1600 1610 1620 1630 1640 1650 1660 1670 1680  
530  
C C A C T A T G C C A A C T A C T C A A T T T T C C C C T C C T A G C A G C A T T C C A T C T T C C G A T C T T T T G C T T C T C C A A C C A A A C A C A T C A A T G T T A T T A G T T C T G T A T A C A G T A C A G G A T C T  
1650 1700 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800  
560  
T T G G T A C T C T A T C A C A G C C C A G T A C C A C A C T C A T C A G A G A A A G A C A G A G A G T A G C T G A G A G C T A A A A C T A C T A C C T T T T C C C T A C C C T A T T C C T C A A T C T T T  
1810 1820 1830 1840 1850 1860 1870 1880 1890 1900 1910 1920  
590  
T A C C T T T T C A A A T C C C A A T C C C A A T C A G T T T T C T C T T T C T T A C T C C C T C T C C C T T T A C C T C C A T G T T A A G G A G A G A T G G G A G A C A T C A T T C T G T T A T A C T T C T G T A C  
1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030 2040  
620  
A C A G T T A C A T G C T A T C A A A C C C A G A C T T G C T T C C A T A G T G S G G A C T T G C T T T T C A G A A C A T A G G A T G A A A G T T T G G G G A A A A G T T T C T T T C A G A G A G A T T A  
2050 2060 2070 2080 2090 2100 2110 2120 2130 2140 2150 2160



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[illegible]

GCCATTCTAAGACCTTGTATGTTATGGAGGTCYGAQAGGCATGATTTGACGAAGCATTGGCATAATCAATTGTAACATAAAAAGCTGACATTTGACCAGACATATTGTACTCTTTCT  
2250    2300    2310    2320    2330    2340    2350    2360    2370    2380    2390    2400

TAA	2419
AAA	2420
AAT	2421
ATA	2422
TAAT	2423
CTAC	2424
GAGAA	2425
GAAGA	2426
C AACCG	2427
TT CGTTCG	2428
TTTGCA	2429
ATCTAC	2430
AGCTAG	2431
TAGAG	2432
ACTTTG	2433
AGACATT	2434
YGAGGA	2435
GAATTC	2436
ACACAG	2437
TGTCTT	2438
CAGCAG	2439
TGTCTT	2440
CAGAGC	2441
CAAGCA	2442

AGAGTTCAAGTGGCTAGACCAGGACATAGTATCATGCTCTCTTTAACTAGCATACCCCAAGTGGAGAAGGGTGCAGCAGGCTCAAAGGCATAAAGTCATTTCCAAATCAGCCAACTA  
2530 2540 2550 2560 2570 2580 2590 2600 2610 2620 2630 2640 2650

AGTGTCTCTTTCIGGTTTCGTCCACCATGGACATTTTCTATATAGTTAATCCTCTCTATCTTGAATCTTCTAGAGAGTTCCTGACCAACTGACGTATGTTTCCCTTTTGTAATTAAT

AAAC1EGTCTTC1GGTTCAAA  
2770

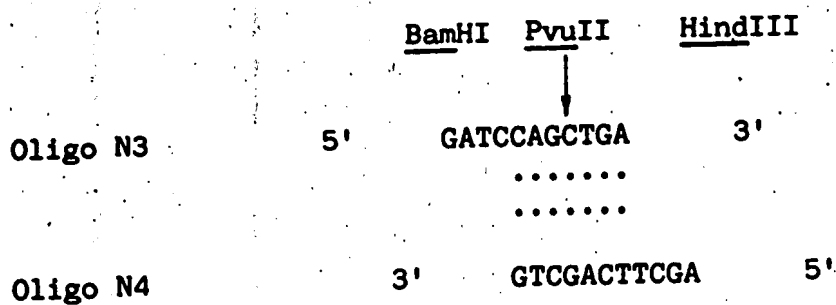


Fig. 10

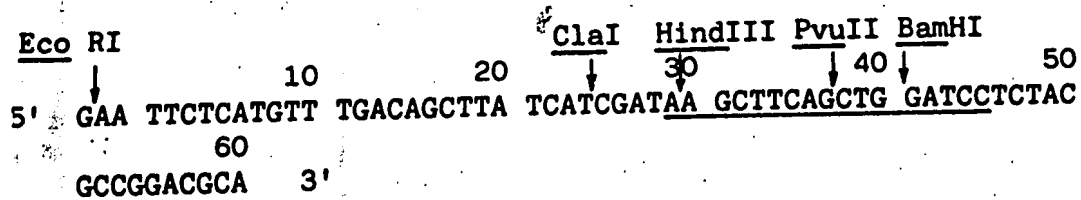
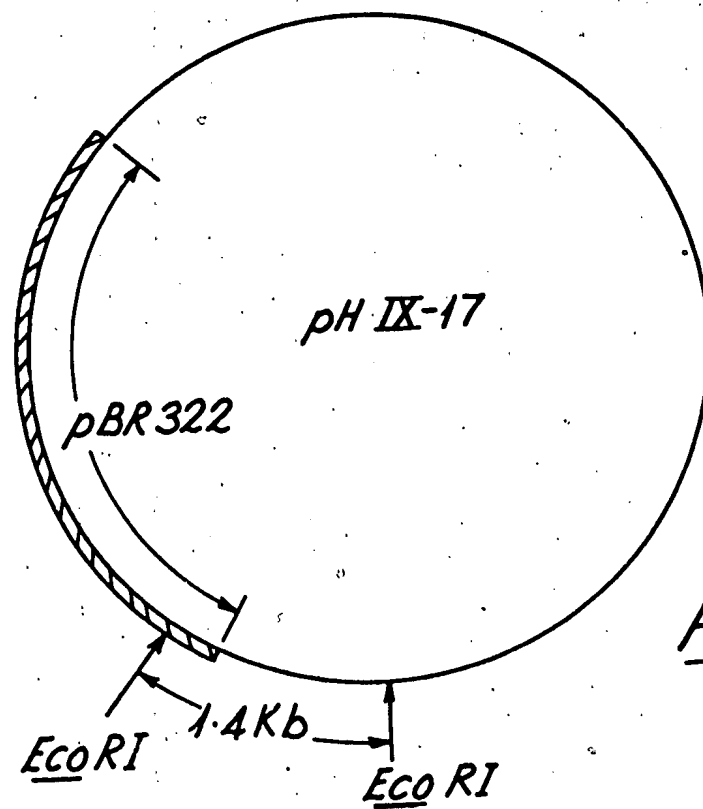
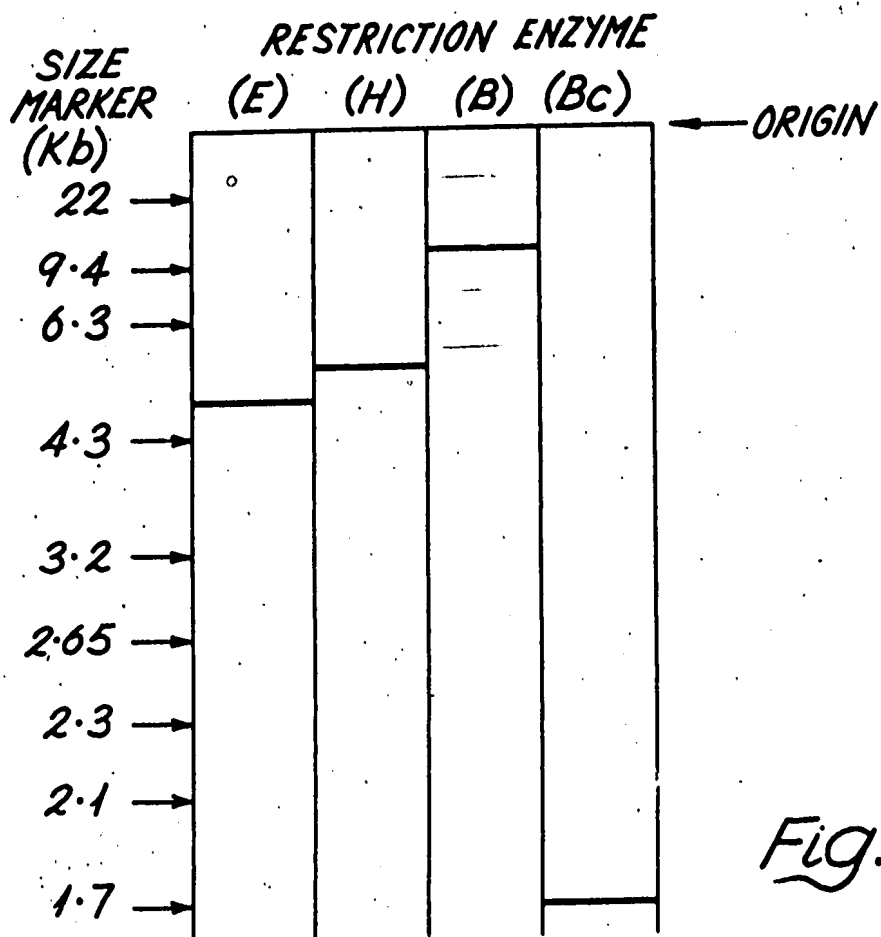


Fig. 11



*Fig. 12*



*Fig. 13*

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